BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

ZEPBOUND® (tirzepatide) subcutaneous injection for obstructive sleep apnea (OSA) Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Purpose: This coverage guideline is used to review Zepbound use in established obstructive sleep apnea (OSA). For use in weight loss, please refer to the member's benefit plan book.

Criteria:

- **Criteria for initial therapy:** Zepbound (tirzepatide) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with Pulmonologist or Sleep Medicine Physician

  2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of **moderate to severe obstructive sleep apnea (OSA)** in an individual with obesity (BMI of 95th percentile or greater or BMI 30 kg/m^2 or greater)

4. Individual has a **baseline** apnea-hypopnea index ≥ 15 events/hour on polysomnogram

5. Individual is using Zepbound in combination with a program supporting a reduced calorie diet, at least 500 kcal/day reduction in intake, and physical activity of at least 150 minutes per week

6. There are paid claims or submission of medical records (e.g., chart notes) confirming at least a 3-month trial and inadequate response, contraindication, or intolerance to **ONE** non-GLP-1 receptor agonist weight loss medication such as:
    a. Contrave (bupropion / naltrexone)
    b. Orlistat (Alli, Xenical)
    c. Phentermine
    d. Qsymia (phentermine / topiramate ER)

7. Individual is not using Zepbound concurrently with a GLP-1 agonist (e.g., Ozempic, Rybelsus, Trulicity, Mounjaro, etc.) as the efficacy and safety of combination anti-obesity therapy for weight loss is not known

8. Individual does not have a diagnosis of diabetes mellitus type 1 or type 2, history of ketoacidosis, hyperosmolar state/coma, or HbA1c greater than 6.5%

9. Zepbound is **NOT** solely being used for weight loss, individual **must** also be on appropriate therapy for **OSA**

10. **For OSA:** Individual is using Positive Airway Pressure (PAP) therapy unless there is medical or other justification against its use such as:
    a. Develops skin reactions and skin irritation from the device
    b. Significant nasal polyposis, congestion or dryness that is unresponsive to nasal therapies
    c. Eye irritation from pressurized air
    d. Aerophagia (air swallowing)
    e. Air leakage around the device
    f. Psychosocial issues such as claustrophobia, noncompliant personality, alcohol or drug abuse, and psychiatric disorders
    g. Other (e.g., facial hair, improper device placement due to arthritis or muscle weakness, etc.)

11. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

12. There are **NO** FDA-label contraindications such as:
    a. Personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2)
    b. A prior serious hypersensitivity reaction (e.g., anaphylaxis, angioedema) to Zepbound or to GLP-1 receptor agonists

13. Individual does **NOT** have **ANY** of the following:
    a. Severe gastrointestinal disease including severe gastroparesis

b. Suicidal behavior or ideation
c. Signs and symptoms of pancreatitis
d. Gallbladder disease such as cholelithiasis, cholecystitis
e. Individual of childbearing potential is pregnant

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Zepbound (tirzepatide) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with Pulmonologist or Sleep Medicine Physician

2. Individual has documentation of positive clinical response to therapy defined as **BOTH** of the following:
   a. Achieves and maintains an improvement in AHI over baseline
   b. Achieves and maintains a reduction of 5% or more in body weight from baseline

3. Individual has been adherent with the medication and continues a program supporting a reduced calorie diet, at least 500 kcal/day reduction in intake, and physical activity of at least 150 minutes per week

4. There are paid claims or submission of medical records (e.g., chart notes) confirming at least a 3-month trial and inadequate response, contraindication, or intolerance to **ONE** non-GLP-1 receptor agonist weight loss medication such as:
   a. Contrave (bupropion / naltrexone)
   b. Orlistat (Alli, Xenical)
   c. Phentermine
   d. Qsymia (phentermine / topiramate ER)

5. Individual is not taking Zepbound in combination with GLP-1 agonists (e.g., Ozempic, Rybelsus, Trulicity, Mounjaro, etc.) as the efficacy and safety of combination anti-obesity therapy for weight loss is not known

6. Individual does not have a diagnosis of diabetes mellitus type 1 or type 2, history of ketoacidosis, hyperosmolar state/coma, or HbA1c less than 6.5%

7. Zepbound is **NOT** solely being used for weight loss, individual **must** also be on appropriate therapy for **OSA**

8. **For OSA:** Individual is using Positive Airway Pressure (PAP) therapy unless there is medical or other justification against its use such as:
   a. Develops skin reactions and skin irritation from the device
   b. Significant nasal polyposis, congestion or dryness that is unresponsive to nasal therapies
   c. Eye irritation from pressurized air
   d. Aerophagia (air swallowing)
   e. Air leakage around the device
   f. Psychosocial issues such as claustrophobia, noncompliant personality, alcohol or drug abuse, and psychiatric disorders

g. Other (e.g., facial hair, improper device placement due to arthritis or muscle weakness, etc.)

9. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

10. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Pancreatitis
        ii. Severe hypersensitivity reaction (e.g., anaphylaxis and angioedema)
        iii. Acute kidney injury
        iv. Severe gastrointestinal disease (e.g., gastroparesis)
        v. Drug induced immune-mediated thrombocytopenia
        vi. Acute gallbladder disease (e.g., cholelithiasis, cholecystitis)

11. Individual does **NOT** have **ANY** of the following:
    a. Severe gastrointestinal disease including severe gastroparesis
    b. Suicidal behavior or ideation
    c. Signs and symptoms of pancreatitis
    d. Gallbladder disease such as cholelithiasis, cholecystitis
    e. Individual of childbearing potential is pregnant

12. Individual is not currently taking any other drugs which cause severe adverse reactions requiring discontinuation

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Zepbound (tirzepatide) is a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist indicated in combination with a reduced-calorie diet and increased physical activity to treat moderate to severe obstructive sleep apnea (OSA) in adults with obesity.

OSA is the most common type of sleep apnea and is characterized by repeated episodes of complete or partial obstructions of the upper airway during sleep despite the effort to breathe, and is usually associated with a reduction in blood oxygen saturation. In OSA, the episodes of decreased breathing are called “hypopnea”

(defined as a ≥ 30% drop in flow for 10 seconds or longer, associated with ≥ 3% oxygen desaturation). The episodes of breathing cessations are called “apneas” (literally, “without breath”) and are defined, as a ≥ 90% drop in flow for 10 seconds or longer and associated with ≥3 % oxygen desaturation, or an arousal. The number of events per hour are measured and reported as an apnea hypopnea index (AHI).

Moderate to severe OSA, can also be defined as a respiratory disturbance index [RDI] greater than 15 events per hour. Like the AHI, RDI reports on respiratory events during sleep, but unlike AHI, it also includes respiratory-effort related arousals (RERAs). RERAs are arousals from sleep that do not technically meet the definitions of apneas or hypopneas, but do disrupt sleep. They are abrupt transitions from a deeper stage of sleep to a shallower stage. RERA is characterized by increasing respiratory effort (and thus decreasing esophageal pressures) for 10 seconds or more leading to an arousal from sleep, but one that does not fulfill the criteria for a hypopnea or apnea.

Positive airway pressure (PAP) is the treatment of choice for an individual with OSA. A maximal effort to treat OSA with PAP for an adequate period of time should be made prior to initiating pharmacologic therapy.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Apnea Hypopnea Index (AHI):

- The AHI is the number of apneas or hypopneas events per hour of sleep (i.e., apneas + hypopneas/total sleep time in hours)
- It is a measure sleep apnea severity; the apnea must last for at least 10 seconds and be associated with a decrease in blood oxygenation
- Based on the AHI, the severity of OSA is classified as follows:
  - None/Minimal: AHI < 5 per hour
  - Mild: AHI ≥ 5, but < 15 per hour
  - Moderate: AHI ≥ 15, but < 30 per hour
  - Severe: AHI ≥ 30 per hour

Respiratory Disturbance (or distress) Index (RDI):

- Like AHI, it reports on respiratory events during sleep, but unlike AHI, it also includes respiratory-effort related arousals (RERAs) (i.e., (apneas + hypopneas + RERAs/total sleep time in hours)
- RERAs are arousals from sleep that do not technically meet the definitions of apneas or hypopneas but do disrupt sleep. They are abrupt transitions from a deeper stage of sleep to a shallower stage
  - A RERA is characterized by increasing respiratory effort (and thus decreasing esophageal pressures) for 10 seconds or more leading to an arousal from sleep, but one that does not fulfill the criteria for a hypopnea or apnea
- Respiratory Event Index (REI) = apneas + hypopneas/total recording time

Diagnosis obstructive sleep apnea		
Sleep testing device	Index	Diagnostic criteria for OSA

PHARMACY COVERAGE GUIDELINE

ZEPBOUND® (tirzepatide) subcutaneous injection for obstructive sleep apnea (OSA) Generic Equivalent (if available)

Polysomnography*	Apnea Hypopnia Index (AHI)	AHI 5-14/hour sleep **PLUS** one or more sleep-associated conditions¶ **or** AHI ≥15/hour sleep
	Respiratory Disturbance Index (RDI)	RDI 5-14/hour sleep **PLUS** one or more sleep associated conditions¶ **or** RDI ≥15/hour sleep
Home sleep apnea device	Respiratory Event Index (REI)	REI ≥15/hour total recording time

* Most polysomnography studies will report AHI, RDI, or both values

¶ Sleep-associated conditions include the following:

- Sleepiness, nonrestorative sleep, fatigue, or insomnia symptoms
- Waking up with breath holding, gasping, or choking
- Habitual snoring, breathing interruptions, or both noted by a bed partner or other observer
- Hypertension, mood disorder, cognitive dysfunction, CAD, stroke, CHF, atrial fibrillation, or type 2 DM

Resources:

Zepbound (tirzepatide) subcutaneous injection product information, revised by Eli Lilly and Company. 12-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 06, 2025.

Malhotra A, Kundel V. Obstructive sleep apnea: Overview of management in adults. In: UpToDate, Editor(s) (Ed), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2025. Topic last updated December 17, 2024. Accessed February 07, 2025.

Malhotra A, Grunstein RR, Fietze I, et al.: Tirzepatide for the treatment of obstructive sleep apnea and obesity. NEJM 2024 Oct 3;391(13):1193-1205. Accessed February 07, 2025.